165

CLAIMS

What is claimed is:

- 1. An ErbB4 kinase domain in liganded crystalline form, comprising the amino acid sequence of SEQ ID NO: 1 and having the structural coordinates of Table 2.
- 2. A liganded ErbB4 kinase domain as claimed in claim 1, wherein the crystalline form has lattice constants of a = 63.95 Å, b = 63.95 Å, c = 163.95 Å, α = 90°, β = 90°, and γ = 90°.
- 3. A liganded ErbB4 kinase domain in crystalline form as claimed in claim 1, wherein said crystalline form has a space group of P4₃.
- 4. A method of ErbB4 inhibitor design, comprising:

generating a three dimensional computer model which represents ErbB4 kinase domain in liganded form, said kinase domain described by the amino acid sequence of SEQ ID NO: 1 and having the structural coordinates of Table 2;

evaluating compounds as potential ErbB4 inhibitors using said model; and

selecting compounds for further testing based on said evaluation.

5. A method of ErbB4 inhibitor design, comprising:

generating a three dimensional computer model which represents a ErbB4 kinase domain in liganded form, said kinase domain described by the amino acid sequence of SEQ ID NO: 1 and having the structural coordinates of Table 2;

evaluating compounds as potential ErbB4 inhibitors using said model; wherein said evaluation comprises identifying compounds capable of at least one of the following ErbB4 kinase domain/compound interactions:

- (iv) one or more interactions with amino acid residues of the ErbB4 kinase domain hinge region;
- one or more interactions with amino acid residues of the ErbB4 kinase domain adenine pocket,
- (iii) one or more interactions with amino acid residues of the ErbB4 kinase sugar pocket,
- (iv) one or more interactions with amino acid residues of the ErbB4 kinase domain back pocket, and
- (v) one or more interactions with amino acid residues of the ErbB4 kinase domain solvent interface; and

selecting compounds for further testing based on said evaluation.

6. A method of ErbB4 inhibitor design, comprising:

generating a three dimensional computer model which represents a ErbB4 kinase domain in liganded form, said kinase domain described by the amino acid sequence of SEQ ID NO: 1 and having the structural coordinates of Table 2;

evaluating compounds as potential ErbB4 inhibitors using said model; wherein said evaluation comprises identifying compounds capable of at least one of the following ErbB4 kinase domain/compound interactions:

(i) one or more interactions with amino acid residues 796, 797, 798, 799, and 800;

- (ii) one or more interactions with amino acid residues 724, 749, and 850;
- (iii) one or more interactions with amino acid residues 848, 860, 803, 847, 732, and 725;
- (iv) one or more interactions with amino acid residues 732, 749, 751, 796, 861, 860, 772, 781, 783, 794, 796, and 862; and
- (v) one or more interactions with residues 801, 802, 803, 806, and 810; and

selecting compounds for further testing based on said evaluation.

- 7. A method of treating a disorder characterized by inappropriate ErbB4 activity in a mammal, comprising: administering to said mammal a therapeutically effective amount of a compound that can form a complex with a ErbB4 kinase domain thereby resulting in a ErbB4 kinase domain in liganded form, said kinase domain in liganded form being described by the amino acid sequence of SEQ ID NO: 1 and the structural coordinates of Table 2, wherein said complex is characterized by at least one of the following ErbB4 kinase domain/compound interactions:
- (i) one or more interactions with amino acid residues of the ErbB4 kinase domain hinge region;
- (ii) one or more interactions with amino acid residues of the ErbB4 kinase domain adenine pocket,
- (iii) one or more interactions with amino acid residues of the ErbB4 kinase sugar pocket and phosphate region,
- (iv) one or more interactions with amino acid residues of the ErbB4 kinase domain back pocket, and
- (v) one or more interactions with amino acid residues of the ErbB4 kinase domain solvent interface.

- 8. A method of inhibiting ErbB4 in a mammal, comprising: administering to said mammal a therapeutically effective amount of a compound that can form a complex with a ErbB4 kinase domain thereby resulting in a ErbB4 kinase domain in liganded form, said kinase domain in liganded form being described by the amino acid sequence of SEQ ID NO: 1 and the structural coordinates of Table 2, wherein said complex is characterized by at least one of the following ErbB4 kinase domain/compound interactions:
- (i) one or more interactions with amino acid residues of the ErbB4 kinase domain hinge region;
- (ii) one or more interactions with amino acid residues of the ErbB4 kinase domain adenine pocket,
- (iii) one or more interactions with amino acid residues of the ErbB4 kinase sugar pocket and phosphate region,
- (iv) one or more interactions with amino acid residues of the ErbB4 kinase domain back pocket, and
- (v) one or more interactions with amino acid residues of the ErbB4 kinase domain solvent interface.
- 9. An ErbB4 kinase domain/inhibitor complex, comprising: an ErbB4 kinase domain form being described by the amino acid sequence of SEQ ID NO: 1 and the structural coordinates of Table 2 and a compound that can form a complex with the ErbB4 kinase domain said complex is characterized by at least one of the following ErbB4 kinase domain/compound interactions:
- (i) one or more interactions with amino acid residues of the ErbB4 kinase domain hinge region;
- (ii) one or more interactions with amino acid residues of the ErbB4 kinase domain adenine pocket,
- (iii) one or more interactions with amino acid residues of the ErbB4 kinase sugar pocket and phosphate region,

WO 2004/066921 PCT/US2004/001291

169

- (iv) one or more interactions with amino acid residues of the ErbB4 kinase domain back pocket, and
- (v) one or more interactions with amino acid residues of the ErbB4 kinase domain solvent interface.

J